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## parenteral

Word:

Word

Adj. 1. **parenteral** - administered by means other than through the alimentary tract (as by intramuscular or **intravenous** injection)

**medical specialty, medicine** - the branches of medical science that deal with nonsurgical techniques

2. **parenteral** - located outside the alimentary tract

**physiology** - the branch of the biological sciences dealing with the functioning of organisms

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## Opioid Adverse Effects

- Opioids have many possible **adverse** effects; some are common, some not
- Addiction (psychological dependence), **tolerance**, and physical dependence are **not** considered among the **adverse** effects
- The ethical considerations of "double **effect**" and unintended consequences of opioids and other medications is discussed in [Module 10: Common Physical Symptoms](#)
- **Adverse** effects should also be distinguished from **opioid** allergy
  - Many people believe that **opioid-induced**

nausea/vomiting, **constipation**, drowsiness, or even confusion is an allergic reaction

- However, these are not allergic reactions; they are **adverse** effects
- While one or more may present on initial dosing, **adverse** effects can be easily managed and patients generally develop pharmacologic **tolerance** to all but **constipation** within a relatively brief period
- Anaphylactic or true allergic reactions to opioids are rare
  - Urticaria and bronchospasm could be direct **opioid** effects or signs of allergy
  - Sudden onset of breathlessness or other signs of anaphylaxis should be taken very seriously, and the offending **opioid** replaced with another from a different class

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## Common **Adverse** Effects

- **Constipation**
- Dry Mouth
- **Nausea/Vomiting**
- **Sedation**
- Sweats

### **Constipation**

- **Constipation** secondary to **opioid** administration is almost universal
- It is primarily the result of **opioid** effects on the CNS, spinal cord, and myenteric plexus of gut that, in turn:
  - Reduce gut motor activity
  - Increase stool transit time
- The colon has more time to desiccate its contents, leaving large hard stools that are difficult to pass
- Other factors that may make the problem worse include:
  - Dehydration
  - Poor food intake
  - Other medications
- Prevention and management of **opioid**-related

## constipation

- **Tolerance to constipation** may develop very slowly, if at all
- It requires anticipatory and ongoing management
- Dietary interventions alone (e.g., increase fluid and fiber) are often insufficient
- Bulk-forming agents (e.g., psyllium)
  - Require substantial fluid intake
  - Not recommended for those with advanced disease and poor mobility
- To counteract the slowing **effect** of opioids:
  - Start by prescribing a routine stimulant laxative (e.g., senna, bisacodyl, glycerine, casanthranol, etc)
  - Escalate the dose to **effect**
- While stool softeners (e.g., docusate sodium) are not usually effective by themselves, combination stimulant/softeners (e.g., senna + docusate sodium or calcium) can be useful
- Prokinetic agents (e.g., metoclopramide, cisapride, etc) may also significantly counteract the **opioid effect**
- If **constipation** persists, some patients will benefit from the addition of an osmotic agent, such as milk of magnesia, lactulose, or sorbitol, to increase the stool's moisture content
- If the **constipation** proves to be refractory to basic therapy, interventions that are more aggressive may be necessary (see Module 10: Common Physical Symptoms)

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## Nausea, Vomiting

- Many patients starting opioids experience nausea with or without vomiting
  - Young women seem to be most at risk
- These symptoms:
  - Are easily anticipated and treated with antiemetics
  - Usually disappear as **tolerance** develops within a few

days

- Dopamine-blocking agents are most often effective
  - prochlorperazine 10 mg before **opioid** and q 6h
  - haloperidol 1 mg before **opioid** and q 6h
  - metoclopramide 10 mg before **opioid** and q 6h
- In refractory cases, a more aggressive approach or an alternative **opioid** may become necessary (see Module 10: Common Physical Symptoms)

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## Typical Course and Resolution of Sedation

- Patients sometimes complain of feeling sedated or mentally clouded immediately after beginning an **opioid** analgesic
- Care must be taken to distinguish between:
  - True sedation (inability to fully wake up)
  - Exhaustion due to previous sleep deprivation with the unrelieved pain (sleeps a lot, but is able to fully wake up in between)
- **Opioid**-induced sedation usually disappears over a few days as **tolerance** develops
  - Most patients also catch up on their lost sleep over a week or two

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## Sedation in Patients with Advanced Illness

- For patients with very advanced disease, mental clouding and excessive somnolence are often issues
- This is particularly true when patients have multiple concomitant medical conditions, medications, and declining function, even in the absence of **opioid** analgesics
- Pain may, in fact, be the primary stimulant keeping them alert
- Once pain is managed, the patient's "natural" level of sedation may become apparent

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## Management of Sedation

- If sedation occurs:
  - Encourage patients and families to clearly articulate their goals (see Module 7: Goals of Care)
  - Develop a pain management plan that balances alertness and pain control to suit the individual
    - Some patients may prefer to be sleepy and comfortable
    - Others may prefer to be alert and in pain
- If undesired sedation persists:
  - A different **opioid** or an alternate route of administration may provide relief
  - Also, consider the use of a psychostimulant (e.g., methylphenidate 5 mg q am and q noon and titrate), particularly if the **opioid** is providing effective analgesia

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## Uncommon **Adverse Effects**

- Bad Dreams/Hallucinations
- Dysphoria/Delirium
- Myoclonus/Seizures
- Pruritus/Urticaria
- Respiratory Depression
- Urinary Retention

### **Dysphoria/Delirium**

- Delirium due to **opioid** excess may be suggested with the onset of:
  - Confusion
  - Bad dreams
  - Hallucinations
  - Restlessness
  - Agitation
  - Myoclonic jerks
  - Significantly depressed level of consciousness
  - Seizures
- **Opioid-induced delirium** rarely occurs when:
  - **Opioid** dosing guidelines are followed closely
  - Patients have normal renal clearance

- However, one or more of these **adverse** effects may present:
  - Gradually, in the patient who is not passing much urine and is accumulating **opioid** due to decreased intake or dehydration
  - Rapidly, in the patient who is developing sepsis
- For more information, see Module 6: Depression, Anxiety, Delirium

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## Pruritus/Urticaria

- In some patients, opioids produce urticaria or pruritus
- These effects are the result of mast cell destabilization by the **opioid** and subsequent histamine release
- Usually the rash and pruritus can be managed by routine administration of long-acting, nonsedating antihistamines while **opioid** dosing continues
  - fexofenadine 60 mg po bid
  - diphenhydramine, loratadine, or doxepin 10-30 mg po qhs

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## Common Myths about the Respiratory Depression with Opioid Use

**Myth #1:** The risk of respiratory depression when using opioids to relieve pain is high

### The Facts:

- The inappropriate application of animal and human models from acute pain research is in part responsible for this common fear
- Pain is a potent stimulus to breathe
- Pharmacologic **tolerance** to respiratory depression develops quickly
- **Opioid** effects are quite different from those experienced by a patient who is not in pain and receives similar doses

**Myth #2:** As doses increase, respiratory depression can occur



suddenly in the absence of overdose

### The Facts:

- Somnolence always precedes respiratory depression
- Adequate ongoing assessment and appropriate titration of opioids based on pharmacological principles will prevent misadventures
- Patient-controlled analgesia with an appropriate dosing interval (10-15 minutes if iv, 30 minutes if sc) can be used safely, because the patient who takes too many extra doses of **opioid** will fall asleep and stop pushing the button before respiratory depression occurs

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## Management of Respiratory Depression

- If respirations are compromised (< 6/minute), naloxone may be necessary if it is the goal of care to keep the patient alert while treating the underlying cause
  - Dilute 0.4 mg of naloxone to 10 mL with sterile water
  - Administer 0.1 to 0.2 mg IV q 1 to 2 min until the patient is alert
  - As the effective plasma half-life is short (10 to 15 min) due to naloxone's high affinity for lipids, monitor the patient closely every few minutes for recurrent drowsiness
  - If drowsiness recurs, repeat dosing as required until the patient is no longer compromised
- If delirium due to **opioid** excess does occur, but respirations are not compromised (> 6/minute):
  - Routine opioids may be stopped
  - Treat the underlying cause of the **adverse** effects until they abate:
    - Ensure appropriate hydration
    - Manage sepsis

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## Nonpharmacologic Pain Management Techniques

- While pharmacologic approaches may be the mainstay of pain management, physicians should consider all available therapies as they develop an individual's plan of care
- Many patients have realized significant relief through:
  - Neurostimulatory techniques
    - TENS (transcutaneous electrical nerve stimulation)
    - acupuncture
  - Physical therapy
    - therapeutic exercises
    - heat and cold
  - Psychological approaches
    - cognitive therapies
    - relaxation, imagery, hypnosis
    - biofeedback
    - behavior therapy
    - psychotherapy
  - Art or music therapy
  - Massage, body work, etc
- Members of the interdisciplinary team, who may be more familiar with nonpharmacologic interventions, can frequently assist the physician to identify and refer patients appropriately

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## Barriers to Effective Pain Management

- Today, pain management remains inadequate in spite of the fact that we have possessed information discussed in this module for over 20 years
- While this inadequacy may reflect inadequate knowledge, it also reflects barriers to pain relief that are pervasive and (in some cases) institutional
- To become effective, we need to overcome real or perceived barriers, including:
  - Beliefs by physicians and other professionals that pain management is not important
  - Poor assessment techniques
  - Inadequate dissemination of the available knowledge
  - Unfounded fear of addiction, **tolerance**, and **adverse effects**
  - Inappropriate regulatory oversight

- To be effective, individual care plans must:
  - Encourage patients to report their pain freely
  - Take into account each patient's willingness to take medication, or not
- In addition to adequate knowledge, health care systems and institutions may need to change in order to facilitate the implementation of the knowledge

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